Independent Study - The Adaptive Immune Response (Chapter 16)

I. Characteristics of the adaptive immune response (chapter 16 introduction)
   a. Memory
   b. Specificity
   c. Discriminates between "healthy self" vs. "dangerous"

II. Strategy of the adaptive immune response (section 16.1)
   a. Primary versus secondary response
   b. Overview of humoral immunity (figure 16.1)
      i. Protective response against extracellular antigens, e.g. bacteria, toxins, viral particles
      ii. Involves B cells, which differentiate to become plasma cells, which secrete antibodies
         1. Antibodies - two functional regions
            a. "arms" of the Y-shaped molecule
            b. "stem" of the Y-shaped molecule
   c. Overview of cellular immunity also known as cell-mediated immunity
      i. Protective response against intracellular antigens (viruses, intracellular bacteria, cancer cells)
      ii. Involves T cells
         1. Cytotoxic \(\rightarrow\) T\(_C\) cells
         2. Helper \(\rightarrow\) T\(_H\) cells

III. Anatomy of the lymphoid system (section 16.2)
   a. Lymphatic vessels (figures 16.3, 28.1 and 16.2) - Collect fluid and white blood cells from tissues
   b. Secondary lymphoid organs - Where lymphocytes "hang out" to encounter antigens
      i. lymph nodes
      ii. spleen
      iii. mucosal associated lymphoid tissue
         1. Peyer’s patches – M cells sample material in the intestine
      iv. skin-associated lymphoid tissue
   c. Primary lymphoid organs - Where lymphocytes develop
      i. bone marrow
      ii. thymus

IV. The nature of antigens (section 16.3)
   a. Proteins - epitopes/antigenic determinants (figure 16.4)
   b. Polysaccharides (molecules w/repeating identical subunits)

V. The nature of antibodies (section 16.4)
   a. Structure and properties of antibodies
i. Basic structure: Y-shaped molecule
ii. Fab regions – antigen-binding regions
iii. Fc region – “red flag”
iv. Four polypeptide chains - two heavy chains (H), two light chains (L)
v. Variable region
vi. Constant region

b. Protective outcomes of antibody-antigen binding (figure 16.6)
c. Immunoglobin classes (isotypes)

<table>
<thead>
<tr>
<th>Class and Structure</th>
<th>Structure</th>
<th>Percent of Total Serum</th>
<th>Properties and Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgM 970,000</td>
<td>Pentamer</td>
<td>5%–15% (10 days)</td>
<td>First antibody produced during the primary immune response. Only class produced in response to T-independent antigens. Provides direct protection by neutralizing viruses and toxins, immobilizing microorganisms, preventing the adherence of microbes to cell surfaces, and agglutinating/precipitating antigens. Binding of IgM to antigen leads to activation of the complement system (classical pathway).</td>
</tr>
<tr>
<td>IgG 149,000</td>
<td>Monomer</td>
<td>80%–85% (21 days)</td>
<td>Most abundant class in the blood and tissue fluids. Provides long-term protection because of its long half-life. Transported across the placenta, providing protection to the developing fetus; long half-life extends the protection through the first several months after birth. Provides direct protection by neutralizing viruses and toxins, immobilizing microorganisms, preventing the adherence of microbes to cell surfaces, and agglutinating/precipitating antigens. Binding of IgG to antigen activates phagocytes, leads to activation of the complement system (classical pathway) and elicits antibody-dependent cellular cytotoxicity.</td>
</tr>
<tr>
<td>IgA monomer 190,000, secretory IgA 360,000</td>
<td>Dimer in secretions</td>
<td>10%–13% (5 days)</td>
<td>Most abundant class produced, but the majority is secreted into mucus, tears, and saliva, providing mucosal immunity. Also found in breast milk, protecting the intestinal tract of breast-fed infants. Protects mucous membranes by neutralizing viruses and toxins, immobilizing microorganisms and preventing attachment of microbes to cell surfaces.</td>
</tr>
<tr>
<td>IgD 184,000</td>
<td>Monomer</td>
<td>&lt; 1% (3 days)</td>
<td>Involved in the development and maturation of the antibody response. Functions in serum have not been clearly described.</td>
</tr>
<tr>
<td>IgE 188,000</td>
<td>Monomer</td>
<td>&lt; 0.01% (2 days)</td>
<td>Binds via the Fc region to mast cells and basophils; this bound IgE allows those cells to detect parasites and other antigens and respond by releasing their granule contents. Involved in many allergic reactions.</td>
</tr>
</tbody>
</table>

VI. Clonal selection and expansion of lymphocytes (section 16.5; figure 16.8)
  a. Basic principles are true for both B cells and T cells
  b. Naïve lymphocytes – have a receptor but have not “seen” antigen
     i. ~1/2 billion naïve B cells, recognizing ~100 million different epitopes; those that recognize self are eliminated during development
  c. Activated lymphocytes – able to proliferate; have received confirmatory signals
  d. Effector lymphocytes – endowed with specific protective attributes (plasma cells = effector B cells)
  e. Memory lymphocytes – long-lived; ready to become effector cells
VII.  **B Lymphocytes and the antibody response** (section 16.6)

a. The response to T-dependent antigens (figure 16.9)
   i. Most common type of response; primarily protein antigens
   ii. Requires assistance of T-helper cells (T\(_H\) cells)
   iii. B cell processes/presents antigen to T\(_H\) cells for “inspection” in order to gain second opinion
   iv. If a T\(_H\) cell recognizes a fragment being presented, it delivers cytokines that activate the B cell
   v. If no T\(_H\) cell recognizes antigen, the B cell becomes unresponsive
b. Characteristics of the primary response
   i. affinity maturation - mutation fine tunes the fit (figure 16.12)

![Diagram of primary response]

   ii. class switching - IgM → IgG (or IgA or IgE) (figure 16.13)

![Diagram of class switching]

   iii. formation of memory cells

c. Characteristics of the secondary response (figure 16.10)
   i. swifter response (due to memory cells)
      1. primarily IgG in blood/tissues
      2. mucosal response is IgA
   ii. more effective response (due to affinity maturation)
   iii. continued fine-tuning
VIII. General characteristics of T cells (p. 380 - 481; table 16.2)
   a. T-cell receptor (figure 16.15)
      i. Similar in concept to a B cell receptor
         1. Variable region
         2. Constant region
      ii. Does not bind “free” antigen
   b. Effector T cells do not produce antibody, instead, they interact with target cells
      i. Deliver signals to target cells (review figure 16.9 for an example)
   c. Antigen presentation
      i. A “self” cell processes, presents antigen to T cell
         1. Dendritic cells do this to activate T cells
         2. Other cells do this to become target cells (review figure 16.9 for an example)
      ii. Endogenous antigens are presented in MHC class I molecules
      iii. Exogenous antigens are presented in MHC class II molecules (review figure 16.9 as an example)
   d. Antigen recognition (figure 16.17 - study this carefully)
      i. Cytotoxic T cells recognize antigen in MHC class I molecules
      ii. Helper T cells recognize antigen in MHC class II molecules (review figure 16.9 as an example)
   e. CD markers (see figure 16.17)
      i. Helper T cells have CD4 (CD4+ T cells)
      ii. Cytotoxic T cells have CD8 (CD8+ T cells)

IX. Activation of T cells (p. 381 - 382) - The role of dendritic cells (figure 16.18)
   a. In tissues – antigen-capturing
   b. In secondary lymphoid organs – antigen-presenting to naïve T cells, in BOTH MHC class I and MHC class II molecules
   c. Migrate to secondary lymphoid organs
   d. Co-stimulatory molecules expressed when "danger" is sensed
X. Functions of $T_C$ (CD8\(^{+}\)) Cells (p. 382 - 383) (figure 16.19)(see left hand figure below)
   a. Recognize antigen presented by Major Histocompatibility Complex (MHC) Class I
      i. found on all nucleated cells
      ii. endogenous proteins (i.e. made by the cell) are presented
   b. Induce apoptosis in corrupt “self” cells (ex. virally infected)
   c. Secrete cytokines; some increase surveillance of neighboring cells (↑ MHC Class I expression)

XI. Functions of $T_H$ (CD4\(^{+}\)) Cells (p. 383)(Figure 16.9 and right hand figure above)
   a. “Helps” other cells and orchestrates response by producing cytokines to direct other cells
   b. Recognizes antigen presented by MHC Class II
      i. exogenous proteins (i.e. those that have been taken up by the cell) are presented
      ii. found on antigen presenting cells (macrophages, B cells and dendritic cells)
   c. Multiple types – $T_H1$, $T_H2$, and others (don’t need to know these)
   d. B cell activation (B cell as the Antigen Presenting Cell (APC))(figure 16.9)
      i. Presented peptides are parts of material that the B cell’s receptor has recognized
      ii. $T_H$ cells direct cytokines to that B cell, activating it/enabling it to:
          1. multiply and differentiate to form antibody-secreting plasma cells
          2. undergo class switching
          3. produce of memory cells
   e. Macrophage activation (macrophage as the APC) (figure 16.20)
      i. Antigen represents material that the phagocyte has engulfed
          1. $T_H$ cell: directs cytokines to that macrophage to activate macrophage
          2. $T_H$ cell: secretes cytokines that stimulate activated cytotoxic T cells
XII. **Review** (figure 16.17)

XIII. **The Big Picture** (see figure 16.21)

XIV. **Study Questions**

1. The immune system has "memory"; what does this mean?
2. Why is it important for the immune system to distinguish between "healthy self" and "dangerous"?
3. What is the role of the humoral response in adaptive immunity?
4. What is the role of the cellular response in adaptive immunity?
5. Describe some extracellular antigens
6. Describe some intracellular antigens.
7. Which cell type is programmed to make antibodies?
8. Describe the function of the two parts of an antibody molecule.
9. What is the general role of T<sub>C</sub> cells?
10. What is the general role of T<sub>H</sub> cells?
11. What is lymph and where does it originate?
12. What are the primary lymphoid organs, and what is their function?
14. Describe the protective outcomes of antibody-antigen binding.
15. Describe the unique characteristics of IgG, IgM and IgA antibodies.
16. Describe the critical features of clonal selection and expansion.
17. How does affinity maturation lead to a more effective antibody response?
18. How does class switching lead to a more appropriate antibody response?
19. How is the secondary response different from the primary response?
20. Why is the secondary response medically relevant?
21. Compare and contrast the B cell receptor and the T cell receptor.
22. Describe antigen presentation.
23. Compare and contrast the roles of MHC class I molecules and MHC class II molecules.
24. Which T cells have CD4, and which have CD8?
25. Describe the role of dendritic cells in B cell activation.
26. Which cells express MHC class I, and to which T cell type do they present antigen?
27. Which cells express MHC class II, and to which T cell type do they present antigen?
28. How does a T<sub>C</sub> cell determine if a "self" cell is infected ("corrupt")?
29. Compare and contrast the outcome of antigen recognition by a T<sub>C</sub> cell versus a T<sub>H</sub> cell.
30. Compare and contrast T-dependent antigens and T-independent antigens.